HIV AND THE COLORECTAL MUCOSA - INVESTIGATING THE EARLY INTERACTIONS OF HIV WITH MUCOSAL TARGET CELLS I*N SITU*

Heeva Baharlou[1], Toby Plasto[1 2], Emma Wanicek[3], Melissa Churchill[3], Jacob Estes[4], Anthony Cunningham[2], Andrew Harman[2]

1 School of Medicine, Sydney University, Sydney, Australia
2 Centre for Virus Research, The Westmead Institute for Medical Research, Sydney, Australia
3 Human Biosciences, RMIT, Melbourne, Australia
4 Vaccine and Gene Therapy Institute, OR, USA

There is no vaccine for HIV. Antiretroviral therapy has helped reduce transmission rates, but alone is not enough to combat this significant global health issue. As such, we need to develop strategies to block transmission of the virus to complement current therapies. This requires an in depth understanding of early viral pathogenesis across the human anogenital tract, of which there is limited data.

In this study we infected human colorectal explant tissues and have performed an extensive analysis of HIV spread within the colorectal mucosa within minutes to hours post infection. To do this we have combined a new in situ hybridisation technology called RNAscope, with highly multiplexed microscopy to compare HIV uptake and transfer kinetics across multiple known HIV target cells including Dendritic Cells (DC), Macrophages and T cells, all in a single tissue section.

Our results show that both DCs and CD4 T cells are able to take up HIV rapidly, within 30min post-infection, however macrophage involvement does not occur until 2h post-infection. Furthermore, we have observed HIV in association with DC-T cell conjugates with the frequency of these contacts increasing with time. We devised several image analysis algorithms which show that in fact the majority of HIV resides within DC-T cell conjugates within the mucosa early post-infection. Although previously hypothesised, to our knowledge this is the first demonstration of DC involvement in early viral transfer to T cells within the mucosa.

We have also examined HIV entry into rectal lymphoid aggregates which are a known site of HIV latency, but unstudied in the context of HIV transmission. Our results show that within just 30min, HIV is able to enter both the T and B cell zones of these structures, associating with CD4 T cells and follicular DCs respectively, potentially indicating rapid seeding of the viral reservoir.

Overall, we show that initial HIV dissemination is rapid, involving multiple cell types which may interact to facilitate viral spread.